

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	7	"634740".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:23
L2	194	"fluorescent resonance energy transfer" and 435/6.ccls.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:26
L3	134	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:51
L4	130	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:28
L5	18	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:30
L6	0	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and modification same histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:30
L7	0	"fluorescent resonance energy transfer" and 435/6.ccls. and covalent and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:31
L8	0	"fluorescent resonance energy transfer" and 435/6.ccls. and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:31
L9	0	"fluorescent resonance energy transfer" and histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32
L10	49	"fluorescent resonance energy transfer" and histone and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32
L11	7732	histone and modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32
L12	648	histone same modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:32

L13	33	histone same modification and FRET	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:33
L14	51	histone same modification and FRET or fluorescence with resonance with modification	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:35
L15	33	histone same modification and (FRET or fluorescence with resonance with modification)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:35
L16	5	"634740".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:50
L17	7	"634740".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:50
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L19	0	"fluorescent resonance energy transfer" and 435/6.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L20	48	"fluorescent resonance energy transfer" and 435/69.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
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L22	51	"fluorescent resonance energy transfer" and 435/320.1.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:52
L23	1	"fluorescent resonance energy transfer" and 435/194.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:53
L24	1	"fluorescent resonance energy transfer" and 530/358.ccls. and covalent	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 16:53

S1	2	"6639063".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/01/31 12:56
S2	5750	FRET	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:09
S3	249	FRET and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:09
S4	456	"fluorescent resonance energy transfer"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/07/26 15:25
S5	47	"fluorescent resonance energy transfer" and histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:11
S6	0	"fluorescent resonance energy transfer" same histone	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/01 15:11
S7	0	"09865291".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/02 09:53
S8	4	"865291".ap.	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/02 09:53
S9	282	"I5" and histones	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2005/02/03 15:18

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FICATION AND COVALENT

=> ("fluorescent resonance energy transfer" or FRET) and histone and modification
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2 FILE WPINDEX

14 FILES HAVE ONE OR MORE ANSWERS, 74 FILES SEARCHED IN STNINDEX

L2 QUE ("FLUORESCENT RESONANCE ENERGY TRANSFER" OR FRET) AND HISTONE AND MODI
FICATION

=> d rank
F1 263 USPATFULL
F2 21 USPAT2
F3 2 ESBIOBASE
F4 2 IFIPAT
F5 2 SCISEARCH
F6 2 WPIDS
F7 2 WPINDEX
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F9 1 BIOTECHABS
F10 1 BIOTECHDS
F11 1 CAPLUS
F12 1 CEABA-VTB
F13 1 FEDRIP
F14 1 MEDLINE

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=> ("fluorescent resonance energy transfer" or FRET) and histone and modification
L3 9 ("FLUORESCENT RESONANCE ENERGY TRANSFER" OR FRET) AND HISTONE
AND MODIFICATION

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L4 ANSWER 1 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on
STN
TI A fluorescence resonance energy transfer-based probe to monitor nucleosome
structure

L4 ANSWER 2 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN
TI GENETICALLY ENCODED FLUORESCENT REPORTERS OF KINASE, METHYLTRANSFERASE,
AND ACETYL-TRANSFERASE ACTIVITIES

L4 ANSWER 3 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN
TI CHEMICAL MODIFICATION OF DNA USING PEPTIDE NUCLEIC ACID CONJUGATES; PEPTIDE NUCLEIC ACIDS LINKED TO PEPTIDES WHICH HYBRIDIZE TO DNA AND CAN BE USED TO MONITOR THE INTRACELLULAR LOCATION OF EXOGENOUS TRANSFECTED DNA AND TO PROMOTE VARIOUS INTRACELLULAR PROCESSES

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
TI Genetically encoded fusion protein fluorescent reporters of kinase,
methyltransferase, and acetyltransferase activities in cells and tissues

L4 ANSWER 5 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on
STN
TI A genetically encoded fluorescent reporter of histone
phosphorylation in living cells

L4 ANSWER 6 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on
STN
TI Modulation of DNA conformations through the formation of alternative
high-order HU-DNA complexes

L4 ANSWER 7 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1
TI Interaction of maize Opaque-2 and the transcriptional co-activators GCN5 and ADA2, in the modulation of transcriptional activity

L4 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Selective recognition of acetylated **histones** by bromodomain proteins visualized in living cells.

=> d ab bib 1, 2, 4, 5, 8

L4 ANSWER 1 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AB Nucleosomes are the basic units of eukaryotic chromatin structure. By restricting factor access to regulatory DNA sequences, nucleosomes significantly impact genomic processes such as transcription, and various mechanisms to alter nucleosome structure to relieve this repression have evolved. Both nucleosomes and processes that alter them are inherently dynamic in nature. Thus, studies of dynamics will be necessary to truly understand these relief mechanisms. We describe here the characteristics of a novel fluorescence resonance energy transfer-based reporter that can clearly signal the formation of a canonical nucleosome structure and follow conformational and compositional changes in that structure, both at the ensemble-average (bulk) and at the single molecule level. Labeled nucleosomes behave conformationally and thermodynamically like typical nucleosomes; thus they are relevant reporters of nucleosome behavior. Nucleosomes and free DNA are readily distinguishable at the single-molecule level. Thus, these labeled nucleosomes are well suited to studies of dynamic changes in nucleosome structure including single-molecule dynamics. © 2005 Elsevier Inc. All rights reserved.

AN 2005:525011 SCISEARCH
GA The Genuine Article (R) Number: 926KR
TI A fluorescence resonance energy transfer-based probe to monitor nucleosome structure
AU Lovullo D; Daniel D; Yodh J; Lohr D; Woodbury N W (Reprint)
CS Arizona State Univ, Dept Chem & Biochem, Tempe, AZ 85287 USA (Reprint); Midwestern Univ, Coll Osteopath Med, Div Basic Sci, Glendale, AZ 85308 USA; Arizona State Univ, Biodesign Inst, Tempe, AZ 85287 USA nwoodbury@asu.edu
CYA USA
SO ANALYTICAL BIOCHEMISTRY, (1 JUN 2005) Vol. 341, No. 1, pp. 165-172.
ISSN: 0003-2697.
PB ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DT Article; Journal
LA English
REC Reference Count: 53
ED Entered STN: 2 Jun 2005
Last Updated on STN: 2 Jun 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L4 ANSWER 2 OF 8 IFIPAT COPYRIGHT 2005 IFI on STN
AB The invention provides fusion protein reporter molecules that can be used to monitor protein **modifications** (e.g., **histone modifications**) in living cells, and methods of using the fusion reporter molecules for diagnosing protein-modification-associated disorders (e.g. **histone-modification-associated disorders**). The invention also provides methods of using the fusion protein reporters to identify candidate pharmaceutical agents that effect protein **modification** in cells and tissues, thus permitting identification of candidate pharmaceutical agents for treatment of protein-modification-associated disorders.

AN 10758652 IFIPAT;IFIUDB;IFICDB
TI GENETICALLY ENCODED FLUORESCENT REPORTERS OF KINASE, METHYLTRANSFERASE,
AND ACETYL-TRANSFERASE ACTIVITIES
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PA Massachusetts Institute of Technology (52912)
AG MaryDilys S. Anderson, Ph.D.;Wolf, Greenfield & Sacks, P.C., 600 Atlantic
Avenue, Boston, MA, 02210, US
PI US 2004265906 A1 20041230
AI US 2003-634740 20030805
PRAI US 2002-425578P 20021112 (Provisional)
FI US 2004265906 20041230
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
PARN This application claims priority under 35 U.S.C. (sec) 119 to U. S.
provisional application Ser. No. 60/425,578, filed Nov. 12, 2002.
CLMN 129
GI 7 Figure(s).

FIG. 1 is a diagram that shows the sites of post-translational modification on H3 and H4 tails. (=acetylation, upward-trianglefilled =methylation, and *=phosphorylation. (Adapted from Zhang, Y. and Reinberg, D. Genes and Dev. 15:2343-2360, (2001)).

FIG. 2 shows a schematic design of a fusion protein reporter. FIG. 2A shows a general design of a FRET-based indicator of histone modification state in living cells. The modificationspecific binding domain may be a 14-3-3 or FHA domain for detecting histone phosphorylation, a bromodomain for detecting acetylation, or a chromodomain for detecting methylation. FIG. 2B shows the domain structure of an indicator for detecting acetyltransferase activity. The bromodomain comes from one of several bromodomain-containing proteins. The substrate consists of either the H3 or H4 N-terminal peptide. The acetylationcompetent lysines are underlined. The entire reporter can be fused to localization signals or specialized proteins for targeting to specific enzymes, DNA sequences, or chromatin regions. ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR is an H3 Nterminal peptide (SEQ ID NO:1) and SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT is an H4 N-terminal peptide (SEQ ID NO:2).

FIG. 3 shows diagrams of fusion protein reporter constructs that have been produced. FIG. 3A shows histone acetyltransferase indicator fusion protein reporters and FIG. 3B shows kinase indicator fusion protein reporters.

FIG. 4 shows a diagram of the domain structure of the histone 3 phosphorylation indicator (FIG. 4A). The H3 peptide segment (ARTKQTARKSTGGKAPRKQLATKAARKSAP; SEQ ID NO: 18) of the indicator corresponds to the first 30 amino acids of the H3 protein. The known phosphorylation sites (S10 and S28) are underlined. FIG. 4B is a digitized image of Western blots depicting the phosphorylation state of the original reporter and the four point mutants after 600-minute reactions with Msk1 and ATP at 30 degrees C. As expected, the original reporter and the K49E mutant have phosphate groups at both the S10 and S28 sites, while the other mutants lack one or both of the phosphate marks.

FIG. 5 is a histogram showing the distribution of YFP/CFP emission ratios for 71 nocodazole-treated cells and 131 untreated cells. Nocodazole-treated cells display, on average, higher emission ratios than untreated cells, consistent with increased H3-S28 phosphorylation levels. The experimental mean difference is 0.05, outside the 95% confidence interval for a distribution with standard deviation of 0.0511.

FIG. 6 is a diagram of the domain structure of the H4 acetylation indicator. The H4 peptide shown is SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

FIG. 7 shows a diagram of the domain structure of the H3 methylation

indicator (FIG. 7A; ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18)). The lysine in H3 recognized by the HP 1 chromodomain is underlined. FIG. 7B is a digitized image of an immunoblot with alpha-methyl-H3-K9 antibody showing reporter methylation after 6 hours at 30 degrees C. under the same reaction conditions: 3.5 mu M reporter, 50 mM Tris pH 8.5, 20 mM KCl, 10 mM MgCl₂, 2 mM S-adenosylmethionine (SAM), 1.7 mM DTT, and an undetermined concentration of GST-tagged G9a). With either SAM or G9a left out, no methylation was observed.

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
 AB The invention provides fusion protein reporter mols. that can be used to monitor protein **modifications** (e.g., **histone modifications**) in living cells, and methods of using the fusion reporter mols. for diagnosing **protein-modification-associated disorders** (e.g. **histone-modification-associated disorders**). Reporters are designed by fusing, in order from N- to C-terminus, cyan fluorescent protein (CFP), a binding domain specific for the modified **histone** sequence of interest, a peptide substrate corresponding to the N-terminus of **histone H3** or H4, and yellow fluorescent protein (YFP). **Modification** of the peptide substrate by a kinase, acetyltransferase, or methyltransferase then allows it to form an intramol. complex with the binding domain, increasing fluorescence resonance energy transfer (**FRET**) between the two flanking fluorescent moieties. Removal of the **modification** by a phosphatase, deacetylase, or (if methylation is reversible) demethylase reverses the **FRET** change. This design is optimized empirically to maximize responsivity by interchanging the donor and acceptor or the substrate and binding domain, or by varying the length and content of interdomain spacer sequences (linker sequences). Gcn5-based and TAFAB-based **histone acetylation** reporters are emphasized. The invention also provides methods of using the fusion protein reporters to identify candidate pharmaceutical agents that effect protein **modification** in cells and tissues, thus permitting identification of candidate pharmaceutical agents for treatment of **protein-modification-associated disorders**.

AN 2004:430935 CAPLUS

DN 141:18691

TI Genetically encoded fusion protein fluorescent reporters of kinase, methyltransferase, and acetyltransferase activities in cells and tissues

IN Ting, Alice Y.

PA Massachusetts Institute of Technology, USA

SO PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004044168	A2	20040527	WO 2003-US36059	20031112
	WO 2004044168	C1	20040722		
	WO 2004044168	A3	20041021		
	W: CA, JP				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
PRAI	US 2004265906	A1	20041230	US 2003-634740	20030805
PRAI	US 2002-425578P	P	20021112		
	US 2003-634740	A	20030805		

L4 ANSWER 5 OF 8 Elsevier BIOBASE COPYRIGHT 2005 Elsevier Science B.V. on STN

AB An increase in **FRET** indicates phosphorylation of **histone H3** at serine 28. The protein-based reporter (see picture) responds to phosphorylation through intramolecular complexation between a substrate domain derived from **histone H3** and a linked

phosphoserine-recognition domain. The reporter is also effective inside living mammalian cells. FRET = fluorescence resonance energy transfer.

AN 2004244172 ESBIOBASE
 TI A genetically encoded fluorescent reporter of histone phosphorylation in living cells
 AU Lin C.-W.; Ting A.Y.
 CS Prof. A.Y. Ting, Department of Chemistry, Massachusetts Inst. of Technology, Cambridge, MA 02139, United States.
 E-mail: ating@mit.edu
 SO Angewandte Chemie - International Edition, (24 MAY 2004), 43/22 (2940-2943), 15 reference(s)
 CODEN: ACIEAY ISSN: 1433-7851
 DT Journal; Article
 CY Germany, Federal Republic of
 LA English
 SL English

L4 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 AB Acetylation and other modifications on histones comprise histone codes that govern transcriptional regulatory processes in chromatin. Yet little is known how different histone codes are translated and put into action. Using fluorescence resonance energy transfer, we show that bromodomain-containing proteins recognize different patterns of acetylated histones in intact nuclei of living cells. The bromodomain protein Brd2 selectively interacted with acetylated lysine 12 on histone H4, whereas TAFdblvert250 and PCAF recognized H3 and other acetylated histones, indicating fine specificity of histone recognition by different bromodomains. This hierarchy of interactions was also seen in direct peptide binding assays. Interaction with acetylated histone was essential for Brd2 to amplify transcription. Moreover association of Brd2, but not other bromodomain proteins, with acetylated chromatin persisted on chromosomes during mitosis. Thus the recognition of histone acetylation code by bromodomains is selective, is involved in transcription, and potentially conveys transcriptional memory across cell divisions.

AN 2004:149090 BIOSIS
 DN PREV200400152814
 TI Selective recognition of acetylated histones by bromodomain proteins visualized in living cells.
 AU Kanno, Tomohiko; Kanno, Yuka; Siegel, Richard M.; Jang, Moon Kyoo; Lenardo, Michael J.; Ozato, Keiko [Reprint Author]
 CS Laboratory of Molecular Growth Regulation, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892, USA ozatok@nih.gov
 SO Molecular Cell, (January 16 2004) Vol. 13, No. 1, pp. 33-43. print.
 ISSN: 1097-2765 (ISSN print).
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